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Impact of the US Two-Dose Varicella Vaccination Program on the Epidemiology of Varicella Outbreaks: Data from 9 States, 2005–2012

Jessica Leung, MPH^{1,*}, Adriana S. Lopez¹, Joel Blostein², Nancy Thayer³, Jennifer Zipprich⁴, Anna Clayton⁴, Vicki Buttery⁵, Jannifer Andersen⁶, Carrie A. Thomas⁷, Maria del Rosario⁷, Kurt Seetoo⁸, Tracy Woodall⁹, Rachel Wiseman¹⁰, and Stephanie R. Bialek¹

¹National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA

²Division of Immunization, Michigan Dept. of Community Health, Lansing, MI, USA

³Vermont Department of Health, Burlington, VT, USA

⁴Immunization Branch, California Department of Public Health, Richmond, CA, USA

⁵Vaccine-Preventable Disease Unit, Minnesota Department of Health, St. Paul, MN, USA

⁶Office of Epidemiology, Mississippi State Department of Health, Jackson MS, USA

⁷West Virginia Department of Health and Human Resources, Charleston, WV, USA

⁸Center for Immunization, Maryland Department of Health and Mental Hygiene, Baltimore, MD, USA

⁹Disease Control and Environmental Epidemiology Division, Colorado Department of Public Health and Environment, Denver, CO, USA

¹⁰Infectious Disease Control Unit, Texas Department of State Health Services, Austin, TX, USA

Abstract

Background—A routine 2-dose varicella vaccination program was adopted in 2007 in the United States to help further decrease varicella disease and prevent varicella outbreaks. We describe trends and characteristics of varicella outbreaks reported to CDC during 2005–2012 from 9 states.

Methods—Data on varicella outbreaks collected by 9 state health departments were submitted to CDC using the CDC outbreak reporting worksheet. Information was collected on dates of the outbreak, outbreak setting, and number of cases by outbreak; aggregate data was provided on the numbers of outbreak-related cases by age group, vaccination status, and laboratory confirmation.

Conflicts of Interest: There were no conflicts of interest declared.

^{*}Corresponding author: Jessica Leung, MPH, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, MS A-34, Atlanta, GA 30333, Tel: 404-639-6067, Fax: 404-315-2486, JLeung@cdc.gov.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, US Department of Health and Human Services.

Results—Nine hundred and twenty-nine outbreaks were reported from the 6 states which provided data for each year during 2005–2012. Based on data from these 6 states, the number of outbreaks declined by 78%, decreasing from 147 in 2005 to 33 outbreaks in 2012 (p=0.0001). There were a total of 1,015 varicella outbreaks involving 13,595 cases reported by the 9 states from 2005–2012. The size and duration of outbreaks declined significantly over time (p<0.001). The median size of outbreaks was 12, 9, and 7 cases and median duration of outbreaks was 38, 35, and 26 days during 2005–2006, 2007–2009, and 2010–2012 respectively. Majority of outbreaks (95%) were reported from schools, declining from 97% in 2005–2006 to 89% in 2010–2012. Sixty-five percent of outbreak-related cases occurred among 5–9 year olds, with the proportion declining from 76% in 2005–2006 to 45% during 2010–2012.

Conclusions—The routine 2-dose varicella vaccination program appears to have significantly reduced the number, size, and duration of varicella outbreaks in the U.S.

Keywords

varicella; chickenpox; outbreaks; surveillance; varicella vaccination

Introduction

In 2007, the Advisory Committee on Immunization Practices (ACIP) adopted a recommendation for a routine 2-dose varicella vaccination program in the United States¹. Prior to that, the U.S. had a routine 1-dose varicella vaccination program implemented beginning in 1996. Although the 1-dose program significantly reduced varicella disease burden, especially for severe disease resulting in hospitalizations and deaths, outbreaks continued to be reported, even among elementary school-aged populations with high 1-dose coverage¹⁻⁴. These outbreaks were burdensome and challenging for state health departments to control and investigate. Therefore, one of the rationales for implementation of the routine 2-dose varicella vaccination program was to help further decrease and prevent varicella outbreaks.

Varicella in vaccinated children, also known as breakthrough varicella, can occur in about 15–20% of 1-dose vaccinated children. Breakthrough varicella has been found to be milder than varicella in unvaccinated children⁵. However, these cases are still infectious. Studies have shown that 2 doses of varicella vaccine provide more protection than 1-dose^{6, 7} with a vaccine-effectiveness of approximately 94–98%^{6, 8, 9}. Since implementation of the routine 2-dose varicella vaccination program, additional declines in varicella incidence and outbreaks have been documented in a limited number of states, communities, and health systems. ^{10–13}

We describe the trends and characteristics of varicella outbreaks reported by state health departments to CDC during 2005–2012, the period in which the 2-dose varicella vaccination program was implemented in the United States.

Materials and Methods

We reviewed state outbreak surveillance practices and state-based school entry requirements for varicella vaccination among participating states. Data on varicella outbreaks collected by state health departments were submitted to CDC using the CDC outbreak reporting worksheet http://www.cdc.gov/chickenpox/outbreaks/downloads/appx-a-vor-wksht.pdf. Six states (California, Maryland, Minnesota, Texas, Vermont, and West Virginia) provided data on varicella outbreaks annually to CDC during the entire period 2005–2012. Data from these states were used to describe trends in varicella outbreaks. Data from three additional states (Colorado, Michigan, and Mississippi), which were not available for every year of the study period were included in the analysis of outbreak characteristics.

Varicella outbreaks were defined differently by state and changed across time for some states. Varicella outbreaks were defined as the occurrence of 2–5 cases that are epidemiology-linked (Table 1). For this analysis, we defined a varicella outbreak as 3 cases. States provided information on dates of the outbreak (rash onset dates of the first and the last reported varicella case), outbreak setting, and number of cases by outbreak. Aggregate data were provided on the numbers of cases by outbreak by age group (<1, 1–4, 5–9, 10–14, 15–19, and 20 years), vaccination status (unvaccinated, 1 or 2-doses, unknown), and laboratory confirmation. A laboratory-confirmed outbreak was defined as an outbreak that had 1 case with a positive varicella-zoster virus (VZV) laboratory test. Calendar years were grouped as 2005–2006, 2007–2009, and 2010–2012 to reflect the period before the 2-dose program was implemented, early implementation of the 2-dose program, and later implementation of the 2-dose program.

We used Poisson regression to look at trends during 2005–2012 in the number of outbreaks, size of the outbreak, duration of outbreak, and proportion of laboratory-confirmed outbreaks. We used the Cochrane Armitage trend test to look for trends during the study period in the age distribution of cases, setting, size, and cases by vaccination status and their vaccine doses. We excluded 2 outbreaks which were missing information on outbreak dates from the entire analysis. Two-sided P-values < 0.05 were considered statistically significant. Data were analyzed using SAS 9.3 (SAS Institute Inc., Cary, NC).

Varicella outbreak surveillance practices evolved during the period in which these data were collected (Table 1). Two of the states, Minnesota and West Virginia, participated in CDC-funded projects to strengthen school-based varicella outbreak surveillance during 2009–2012. Beginning in 2009, Minnesota expanded school-based surveillance by adding active outbreak surveillance in 80 schools to their existing passive surveillance in sentinel schools. West Virginia, which began collecting information on varicella outbreaks from schools in 2005, implemented active surveillance in all schools statewide in 2010. The remaining states used passive outbreak surveillance during the study period.

State-based school entry requirements for varicella vaccination also evolved during 2005–2012 (Table 1). Seven states implemented a 1-dose varicella vaccination requirement for Kindergarten entry prior to 2005. Two-dose varicella vaccination requirements for school

entry were implemented in 8 of the states during the study period beginning in 2007 (Table 1).

Results

Nine hundred and twenty-nine outbreaks were reported from the 6 states which provided data for each year during this study period: 417 (45%) from California, 53 (6%) from Maryland, 252 (27%) from Minnesota, 117 (13%) from Texas, 24 (3%) from Vermont and 66 (7%) from West Virginia. One outbreak reported from Texas with 2 cases was excluded from the analysis. The number of outbreaks declined by 78%, decreasing from 147 in 2005 to 33 outbreaks in 2012 (p=0.0001) (Figure 1). For California and Maryland, the average annual number of outbreaks during 2005-2012 decreased over time, from 97 to 12 in California and from 14 to 2 in Maryland. In Minnesota, 1 of 2 states which participated in the CDC-funded varicella outbreak surveillance project, the average annual number of outbreaks decreased from 54 outbreaks before the 2009-2010 school-year to 12 outbreaks in the 2010–2011 school-year even as active surveillance was implemented in 80 schools. In West Virginia, the other state which participated in the varicella outbreak surveillance project, there was an increase in the average annual number of outbreaks reported coincident with implementation of active surveillance with a peak of 21 outbreaks in 2010 compared to 2 in 2009 followed by a decline to 4 in 2012. In Texas, the average annual number of outbreaks increased from 12 in 2005-2006 to 23 in 2007-2009, and then decreased to 8 in 2010–2012. In Vermont, the average annual number of outbreaks was relatively stable across the 3 time periods, with an average of 2-4 outbreaks reported per year.

There were a total of 1,015 varicella outbreaks involving 13,595 cases reported by the 9 states during 2005–2012, including the 929 outbreaks reported by the 6 states described above. The size and duration of outbreaks declined significantly over time (p<0.001). The median size of outbreaks was 12, 9, and 7 cases and the median duration of outbreaks was 38, 35, and 26 days during 2005–2006, 2007–2009, and 2010–2012 respectively. Among states with reporting of outbreaks with <5 cases, the proportion of outbreaks with <5 cases increased to 14.6% (25 outbreaks) in 2010–2012 from 1.6% (6 outbreaks) in 2005–2006 (Table 2). There were 2 large outbreaks with 51 cases reported in 2010–2012. One outbreak has been previously described 14, involved 2 elementary schools and 60 vaccinated cases with 48% 1-dose cases and 52% 2-dose cases. The other large outbreak occurred in a K-8th grade school and involved 55 cases; information on vaccination status was available for 13% of cases, all of whom were vaccinated with 1-dose. The proportion of outbreaks that were laboratory confirmed increased to 16.4% in 2010–2012 from 0.3% in 2005–2006 (p<0.001).

Information on outbreak setting was available for 96% of outbreaks. The majority of outbreaks were reported from schools, although the proportion of outbreaks occurring in schools was slightly lower in 2010–2012 compared to 2005–2006 (89% versus 97%). There were 928 school-associated outbreaks involving 12,334 varicella cases. The median duration of these outbreaks was 34 days (range, 0–206 days) and median size was 10 cases (range, 3–131 cases). The number of outbreaks reported from schools declined from 138 in 2005 to 39 in 2012 (p=0.0001). Overall, 76% (4,938/6,522) of varicella cases with information on

vaccination status were vaccinated. Among these 4,938 vaccinated cases, 57% were 1-dose vaccinees and 6% were 2-dose vaccinees. There were 31 (3%) school-associated outbreaks with laboratory confirmation.

Completeness of information on age of outbreak-related cases increased from 50% (2,897/5,812) in 2005–2006 to 97% (1,712/1,763) in 2010–2012. Although the majority of outbreak-related cases occurred among 5–9 year olds, the proportion of cases in this age group declined from 76% of outbreak-related cases during 2005–2006, to 45% during 2010–2012 (Table 1). There was a corresponding increase in the proportion of cases reported among children <5 and 10 years of age.

Completeness of vaccination information on cases increased over time. Information on vaccination status was available for 40% of cases (2,338/5812) in 2005–2006 increasing to 79% (1,389/1,763) in 2010–2012. Information on number of vaccine doses received was available for 59% (1,078/1,825) of vaccinated cases in 2005–2006 and rose to 91% (837/920) in 2010–2012. We analyzed a subset of data in 2010–2012 with information on the vaccination status for the majority of the cases. There were 121 outbreaks in 2010–2012 for which vaccination status was available for 75% of cases. Among these 121 outbreaks, 68 (56%) outbreaks involved 30% unvaccinated cases, 37 (31%) involved 31–89% unvaccinated cases, and 16 (13%) involved 90% unvaccinated cases. Among the 16 outbreaks involving 90% unvaccinated cases, 11 occurred in schools, 2 in daycares, and 3 in other settings. The median size of these outbreaks was 6 cases (range, 3–28 cases), and the median duration was 22 days (range, 3–105 days). The median proportion of unvaccinated cases was 100% (range, 94%–100%).

Discussion

The number of varicella outbreaks in the 6 states with data for all years of the study period (California, Maryland, Minnesota, Texas, Vermont, and West Virginia) decreased by nearly 80% during the first 6 years since implementation of a recommendation for a routine 2-dose varicella vaccination program. We also observed declines in the size and duration of outbreaks. These data corroborate what has been previously reported from an active surveillance site and one state shortly after implementation of the 2-dose program. In an active surveillance site in California, varicella outbreaks declined 75% in 2007–2010 compared with 2003–2006¹¹. In a report from Connecticut, the number and size of school outbreaks decreased from 42 in 2005–2006 to 2 outbreaks in 2008–2009, with the average outbreak size decreasing from 14 to 5 varicella cases 12. The declines in varicella outbreaks, as well as declines in varicella incidence 11, 12, have occurred as 2-dose varicella vaccination coverage has rapidly increased. Two-dose coverage among 7 year-old children increased from <10% in 2006 to >80% in 2012¹⁵ and reached 94% among Kindergartners in the 2012–2013 school year¹⁶; 2-dose varicella vaccine coverage among adolescents approached 75% in 2012¹⁷. The number of states with a 2-dose varicella vaccination school entry requirement for Kindergarten increased from 4 (8%) states in 2007 to 36 (71%) in 2012¹⁵. Although these decreases in varicella outbreaks were noted before many of these states implemented 2-dose varicella vaccine requirements for school entry, requirements are

important for maintaining high vaccine coverage, which is critical for preventing or curtailing outbreaks.

During the study period, the proportion of cases among children aged < 5 and 10 years increased and may be related to lower 2-dose varicella vaccination coverage in these age groups since the routine 2nd dose is recommended for children aged 4–6 years and the majority of school requirements are targeted for Kindergarten school-entry. We did see a slight increase in the proportion of outbreaks occurring among daycares and in settings other than schools during the study period, including adult facilities such as correctional and healthcare facilities, although the proportion of outbreaks occurring in these settings remained small compared to outbreaks reported in schools. There is likely under-reporting of varicella outbreaks in these other settings because the primary reporting source for outbreak surveillance is schools. In settings at increased risk of VZV transmission and varicella outbreaks, strategies for preventing outbreaks may include surveillance, assessment and documentation of evidence of immunity to VZV¹ in exposed persons, and vaccination of susceptible persons with 2-doses of varicella vaccine.

We found that the majority of varicella outbreaks continued to occur in elementary and middle schools and among vaccinated children 5–14 years of age. However, we also saw an increase in the proportion of outbreak-related cases in unvaccinated children. Of the 121 reported outbreaks during 2010–2012 with complete information on vaccination status of cases, 16 predominantly involved unvaccinated individuals. Although varicella vaccine exemption rates are low nationally (1.8%)¹⁶, clusters of vaccine exemptors exist. Some of the outbreaks with high proportions of unvaccinated cases occurred in schools or communities where vaccine hesitancy is common, but others were reported from schools with high vaccine coverage that may have been driven by multiple cases within a small number of families who were vaccine exemptors. Rates of non-medical vaccine exemption are rising, particularly in states that allow for philosophical exemptions^{18, 19}. These growing pockets of susceptible individuals fuel disease transmission and lead to outbreaks with possibly longer sustained transmission that may result in severe consequences²⁰.

Although varicella outbreaks have declined during the 2-dose varicella vaccine era, they continue to pose a challenge to manage and control^{14, 21}. Outbreaks continue to occur mainly among vaccinated persons, in whom disease can be modified, mild, and difficult to diagnose clinically. It is not clear if there are differences in clinical severity between varicella cases who previously received 1-dose of varicella vaccine compared to those who received 2-doses, although studies of medically attended varicella have reported no significant differences^{11, 14, 21}. It is also unknown whether the contagiousness differs between 1-dose versus 2-dose vaccinated cases, although it seems plausible that the number of lesions would play a role. Nevertheless, because 2-dose vaccinated cases are a potential source of infection, health departments need to continue monitoring varicella cases reported among 1 and 2-dose vaccine recipients and ensure that control measures are implemented as soon as possible to prevent further disease transmission. Better laboratory diagnostics for confirming breakthrough varicella cases are also needed.

There were several limitations to this analysis. The analysis was based on aggregate data and we did not have case-based data on the outbreak-related cases. We were unable to look at individual characteristics of the cases, and thus unable to describe the age distribution or disease severity by vaccination status. Although data on age and vaccination status were missing for a significant proportion of the cases (40% for age and 45% for vaccination status), completeness for these variables significantly improved over time, from 50% to 97% for age and 40% to 79% for vaccination status. Information on lesion severity was collected, but was not reported in this manuscript since information was missing for 90% of cases. Completeness of reporting for outbreak-related variables may continue to improve as the number of outbreaks decline over time and an increased number of states conduct case-based varicella surveillance. Much progress has been made in expanding national varicella surveillance in the United States with varicella now reportable in 44 out of 51 jurisdictions (50 states and DC) as of 2012²².

In conclusion, the routine 2-dose varicella vaccination program appears to have significantly reduced the number, size, and duration of varicella outbreaks in the U.S. Ongoing surveillance is important to continue monitoring the impact of the varicella vaccination program and the epidemiology of varicella outbreaks to better target control and prevention strategies. CDC encourages state health departments to report annual varicella outbreak data to CDC using this form: http://www.cdc.gov/chickenpox/outbreaks/downloads/appx-a-vor-wksht.pdf. With additional increases in 2-dose varicella vaccination coverage and implementation of 2-dose school entry requirements, varicella incidence and outbreaks in the U.S. should continue to decrease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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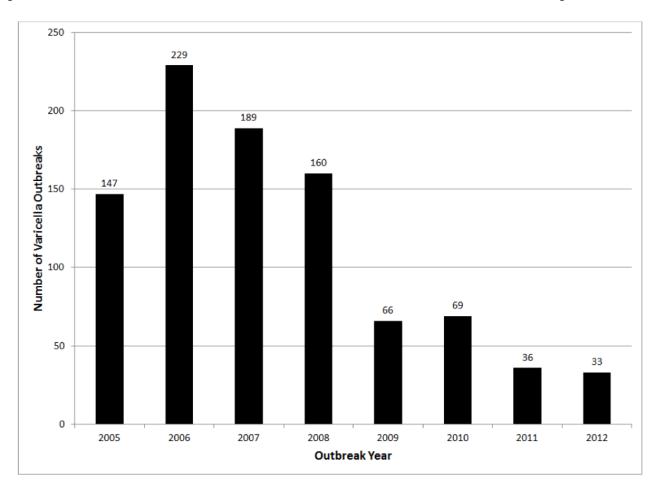


Figure 1. Number of Varicella Outbreaks by Year, Data from 6 States, 2005–2012 $(N\!=\!929$ Outbreaks)^a

^aData from Minnesota in 2005 was only available starting in September 2005.

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Table 1

Summary of varicella outbreak surveillance and varicella immunization school-entry requirements by state

				Varicella immunizat Kindergai	Varicella immunization requirements for Kindergarten entry
State	Type of varicella outbreak surveillance	Definition of varicella outbreak	Years of outbreak surveillance data	Year 1-dose requirement implemented	Year 2-dose requirement implemented
California	passive surveillance	5 cases	2005–2012	2001	
Colorado	passive surveillance	5 cases	2007–2012	2000	2007
Maryland	passive surveillance	3 cases	2005–2012	2001	2014
Michigan	passive surveillance	5 cases	2006–2012	2002	2010
Minnesota	passive surveillance 2005–2012 and active surveillance in a subset of school sentinel sites 2009–2012	5 cases	2005–2012	2004	2009
Mississippi	passive surveillance	2 cases, dependent on setting	2007–2011	2002	2009
Texas	passive surveillance	2 to 5 cases, dependent on setting	2005–2012	2000	2009
Vermont	passive surveillance	5 cases	2005–2012		2008
West Virginia	passive surveillance 2005–2009 and active surveillance 2010–2012	5 cases (during 2010–2011, revised definition to 3 cases)	2005–2012		2008

Leung et al.

 Table 2

 Reported Varicella Outbreaks during 2005–2012, Data from 9 States: Selected Variables

Variable	2005	2005–2006	2007-	2007–2009	2010-	2010-2012	p-value for trend test
	Vari	cella Ou	tbreak D	Varicella Outbreak Data (N=1,015 outbreaks)	,015 out	breaks)	
Total # Outbreaks	387		457		171		
	#	%	#	%	#	%	
$\mathbf{Setting}^a$							
Daycare	7	1.9	∞	1.9	7	4.1	0.0084^{b}
School	367	97.1	410	95.1	151	88.8	0.0014^{b}
Other ^d	4	1.1	13	3.0	12	7.1	$< 0.0001^{b}$
$Total^e$	378	7.76	431	94.3	170	99.4	
Outbreak Size							
<5 cases	9	1.6	16	3.5	25	14.6	$< 0.0001^{b}$
5–9 cases	142	36.7	223	48.8	87	50.9	0.0005^{b}
10-20 cases	159	41.1	147	32.2	42	24.6	0.0001^b
21–50 cases	73	18.9	63	13.8	15	8.8	0.0006b
51 cases	7	1.8	∞	1.8	7	1.2	0.9713^{b}
$Total^{e}$	387	100.0	457	100.0	171	100.0	
		/aricella	Case Da	Varicella Case Data (N=13,595 Cases)	,595 Ca	ses)	
Total # Cases	5,812		6,020		1,763		
	#	%	#	%	#	%	
Age (% among cases with non-missing data) (N=8,059 Cases)	s with no	n-missir	g data) ((N=8,059	Cases)		
<1 year	5	0.2	26	8.0	16	6.0	0.0001^c
1-4 years	93	3.2	126	3.7	115	6.7	$< 0.0001^{b}$
5–9 years	2,187	75.5	2,276	0.99	774	45.2	$< 0.0001^{b}$
10–14 years	589	20.3	961	27.9	699	39.1	$< 0.0001^{b}$
15-19 years	16	9.0	41	1.2	63	3.7	< 0.0001 b

Page 11

Leung et al.

Variable	2005–2006	2006	2007–2009	5000	2010–2012	2012	p-value for trend test
	Varie	ella Out	Varicella Outbreak Data (N=1,015 outbreaks)	ata (N=1	,015 out	breaks)	
Total # Outbreaks	387		457		171		
	#	%	#	%	#	%	
20 years	7	0.2	20	9.0	75	4.4	<0.0001 <i>b</i>
$Total^e$	2,897	49.8	3,450	57.3	1,712	97.1	
Vaccination Status (% among cases with non-missing data) (N=7,454 Cases)	(% amon	g cases 1	vith non-	missing	data) (N	=7,454 (Cases)
Unvaccinated f	513	21.9	992	20.6	469	33.8	$< 0.0001^b$
$Vaccinated^f$	1,825	78.1	2,961	79.4	920	66.2	$< 0.0001^{b}$
$\operatorname{Total}^{arepsilon}$	2,338	40.2	3,727	61.9	1,389	78.8	
Number Vaccine Doses (% among vaccinated cases) (N=3,850 Cases)	ses (% a	mong va	ccinated	cases) (I	V=3,850	Cases)	
1-dose	1,077	59.0	1,838	62.1	613	9.99	0.3588^{b}
2-dose	-	0.1	76	3.3	224	24.3	$< 0.0001^{b}$
$Total^{\mathcal{S}}$	1,078	59.1	1,935	65.3	837	91.0	

 $^{^{\}it a}$ Information on outbreak setting missing for 36 outbreaks.

Page 12

bCochrane Armitage Trend test used.

 $^{^{}c}$ Exact Cochrane Armitage Trend test used.

d Other settings include community, correctional facilities, healthcare facilities, and universities.

 $^{^{\}rho}$ Percentages calculated out of total number of reported outbreaks or cases by study period.

 $f_{
m We}$ excluded those with prior varicella disease if information was available on prior disease history.

 $^{^{\}it g}$ Percentages calculated out of total reported number of vaccinated cases by study period.